

Non-Scientific Abstract:

Cancers of the colon and rectum are the second leading cause of cancer death in the United States and the colon and rectum are the third and fourth most common sites of malignancy in most Western countries. It is estimated that there will be nearly 135,000 new cases of colorectal cancer diagnosed in the United States and this rate has been increasing by approximately 5% each year (1). Rectal cancers present a particular challenge for local control given the anatomic considerations of the pelvis and their propensity to invade into areas around the rectum.

In this protocol, we will combine TNFerade™, an adenoviral gene transfer vector that expresses TNF- α , an anti-cancer protein, with chemoradiation prior to surgery. TNFerade™ contains genetic elements that are controlled by radiation so that the expression of the TNF- α anti-cancer protein is produced at the site of the cancer but not so much gets into the body as to cause toxic side effects. The goal of therapy is to allow for the complete surgical resection of these tumors while preserving sphincter function whenever possible.

The population for this study will be newly diagnosed adult subjects with locally advanced rectal cancer limited to the rectum and regional lymph nodes who have not received prior treatment and are to receive chemoradiation prior to surgery. Patients with metastatic disease at time of screening are not eligible.

Combinations of pre-operative radiation and 5FU based chemotherapy followed by surgery result in complete pathologic responses in roughly 10-25% of cases. This trial is designed to determine if the local injection of TNFerade™ followed by radiation and chemotherapy can improve the complete pathologic response rate when compared to radiation and chemotherapy alone at the time of definitive surgical resection of locally advanced rectal cancers. Secondary endpoints will include disease free and overall survival as well as measurements of local and systemic gene product levels and determinations of changes in gene expression profiles as well as proteomic analysis of tumor tissue prior to, during and following therapy.

(1) Jemal, A., Thomas, A., Murray, T., and Thun, M. Cancer statistics, 2002. CA Cancer J Clin, 52: 23-47, 2002.
